## Functional ultrasound neuroimaging through a human cranial window for decoding of movement effector somatotopy in primary motor cortex

Lydia J. Lin<sup>1,7\*</sup>, Thierri Callier<sup>1</sup>, Charles Y. Liu<sup>1,5,6,8</sup>, Mikhail G. Shapiro<sup>2,3,9</sup>, Richard A. Andersen<sup>1,4</sup>

<sup>1</sup>Division of Biology and Biological Engineering; <sup>2</sup>Division of Chemistry & Chemical Engineering; <sup>3</sup>Andrew and Peggy Cherng Department of Medical Engineering; <sup>4</sup>Tianqiao & Chrissy (T&C) Chen Brain-Machine Interface Center, California Institute of Technology, Pasadena, CA, USA; <sup>5</sup>Department of Neurological Surgery; <sup>6</sup>USC Neurorestoration Center, <sup>7</sup>Keck School of Medicine of USC, Los Angeles, CA, USA; <sup>8</sup>Rancho Los Amigos National Rehabilitation Center, Downey, CA, USA; <sup>9</sup>Howard Hughes Medical Institute, Pasadena, CA, USA \*1200 E. California Blvd, MC 216-76, Pasadena, CA 91125, USA. E-mail: ljlin@caltech.edu

*Introduction:* Brain machine interfaces (BMIs) can help patients with disabilities achieve greater independence by using their thoughts to control assistive devices. However, they commonly require highly invasive brain surgery for electrode implantation while conventional non-invasive imaging techniques like fMRI and EEG lack sufficient spatial resolution for high-bandwidth BMI use. Functional ultrasound (fUS) is a novel neuroimaging technique that balances these tradeoffs and can image from outside the dura with high sensitivity, high spatial resolution, and large field of view [1], demonstrating potential for use in less invasive BMIs. Prior work demonstrated that fUS can be used to decode movement intention in non-human primates [2,3] and task state through a polymeric acoustic skull window in a human patient [4] – the first steps toward enabling a minimally invasive fUS BMI. In this study, we show that fUS can further be used to decode motor effector information from primary motor cortex (M1) in a human participant with an acoustic window implant, demonstrating the growing applications of fUS for BMIs.

*Materials, Methods and Results:* Experiments were performed on a human participant who had previously undergone a hemicraniectomy procedure and polymeric skull reconstruction including an acoustic window. We acquired fUS data from the left M1 as the participant performed randomized instructed movement tasks using different body parts or "effectors" and repeated the movement over a block of time to amplify signal.

We first looked into general effectors – right finger, right wrist, lip, and tongue. Using general linear modelling (GLM) analysis, we identified statistically significant regions of interest (ROIs) linked to each effector, indicating a dorsomedial to ventrolateral distribution for finger, wrist, lip, and tongue, respectively. This matches canonical somatotopic mappings in M1. Furthermore, we found that average fUS activity for these ROIs was tuned to each corresponding effector. Using classwise principal component analysis (CPCA) and linear discriminant analysis (LDA), we were able to significantly decode motor effector at above chance level. We conducted additional experiments on distinguishing contralateral individual finger representation in M1, which requires more refined spatial resolution given the more mixed representation of fingers in M1. Using the same analysis and decoder as the prior experiment, we were similarly able to identify ROIs tuned to each individual finger and significantly decode individual finger movements above chance level.

*Conclusion:* This work demonstrates that fUS is a robust neuroimaging technique that can be used to map and decode movement effector information in a human subject with an acoustic window implant. This presents significant progress in the development of a fUS-based BMI for decoding higher-level functions in humans and highlights the potential of fUS as a minimally invasive alternative for BMIs in the future.

Acknowledgements and Disclosures: We thank participant JH for their devotion that has made this research possible. Funding was provided by the NIH and T&C Chen BMI Center. There are no conflicts of interest.

## References:

 Mace E, Montaldo G, Osmanski BF, Cohen I, Fink M, Tanter M. Functional ultrasound imaging of the brain: theory and basic principles. IEEE Trans Ultrason, Ferroelect, Freq Contr. 2013.

- [2] Norman SL, Maresca D, Christopoulos VN, Griggs WS, Demene C, Tanter M, Shapiro MG, Andersen RA. Single-trial decoding of movement intentions using functional ultrasound neuroimaging. Neuron. 2021.
- [3] Griggs WS, Norman SL, Deffieux T, Segura F, Osmanski BF, Chau G, Christopoulos V, Liu C, Tanter M, Shapiro MG, Andersen RA. Decoding motor plans using a closed-loop ultrasonic brain-machine interface. Nat Neurosci. Nature Publishing Group; 2023.
- [4] Rabut C, Norman SL, Griggs WS, Russin JJ, Jann K, Christopoulos V, Liu C, Andersen RA, Shapiro MG. Functional ultrasound imaging of human brain activity through an acoustically transparent cranial window. Sci Transl Med. 2024.